

27. Gordon P, Griggs RC, Nissley SP, et al: Studies of plasma insulin in myotonic dystrophy. *J Clin Endocr* 29:684-690, 1969
28. Engel WK: Classification of neuromuscular disorders. In *Proceedings of the Second Conference on the Clinical Delineation of Birth Defects*, May 26-30, 1969. New York, The National Foundation, in press
29. Engel WK, Brooke MH: Histochemistry of the myotonic disorders. In Kuhn E (Ed): *Progressive Muskeldystrophie, Myotonic, Myasthenie*. Heidelberg, Germany, Springer-Verlag, 1966, pp 203-222
30. Brooke MH, Engel WK: The histographic analysis of human muscle biopsies with regard to fiber types. 3. Myotonias, myasthenia gravis and hypokalemic periodic paralysis. *Neurology* 19:469-477, 1969
31. Engel WK: Unpublished observations
32. Hathaway PW, Engel WK, Zellweger H: Experimental myopathy after microarterial embolization. *Arch Neurol* 22:365-378, 1970
33. Engel WK: Duchenne muscular dystrophy: A histologically-based ischemia hypothesis compared with experimental ischemia myopathy. In Pearson CF (Ed): *The Pathology of Muscle Disorders*. Baltimore, Williams & Wilkins Co, 1970. In press
34. Olson WH, Engel WK, Walsh GO, et al: Histochemical and ultrastructural changes in limb muscles in patients with progressive external ophthalmoplegia. *Arch Neurol*. To be published
35. Engel WK: Chemocytology of striated annulets and sarcoplasmic masses in myotonic dystrophy. *J Histochem Cytochem* 10:229-230, 1962
36. Hogenhuis LAH, Engel WK: Histochemistry and cytochemistry of experimentally denervated guinea pig muscle: I. Histochemistry. *Acta Anat* 60:39-65, 1965
37. Cöers C, Woolf AL: *The Innervation of Muscle—A Biopsy Study*. Oxford, England, Blackwell Scientific Publications, 1959
38. MacDermot V: The histology of the neuromuscular junction in dystrophia myotonica. *Brain* 84:75-84, 1961
39. Warmolts JR, Engel WK: A critique of the "myopathic" electromyogram. In *Transactions of the American Neurological Association*, 1970, in press
40. Norris FH: Intracellular recording from human striated muscle. In Enslein K (Ed): *Proceedings 2nd Rochester Data Conference*. New York, Pergamon Press, 1963, pp 59-72
41. Li C-L, Engel WK, Klatzo I: Some properties of cultured chick skeletal muscle with particular reference to fibrillation potential. *J Cell Comp Physiol* 53:421-444, 1959
42. Mancall EL, Aponte GE, Berry RG: Pompe's disease (diffuse glycogenosis) with neuronal storage. *J Neuropath Exp Neurol* 24:85-96, 1965
43. Refsum S, Engesest A, Lonnum A: Pneumoencephalographic changes in dystrophia myotonica. *Acta Psychiat Neurol Scand* 34: (Suppl 137): 98, 1959
44. Refsum S, Lonnum A, Sjaastad O, et al: Dystrophia myotonica. Repeated pneumoencephalographic studies in ten patients. *Neurology* 17:345-348, 1967
45. Pleasure DE, Mishler KC, Engel WK: Axonal transport of proteins in experimental neuropathies. *Science* 166:524-525, 1969
46. Griggs RC, Engel WK, Resnick JS: Acetazolamide treatment of hypokalemic periodic paralysis. *Ann Intern Med*. 73:39-48, 1970

Diagnosis and Treatment of Pemphigus

THE REVIEW ON "Recent Advances in the Diagnosis and Treatment of Pemphigus" by Newcomer and Landau printed in this issue emphasizes the important effects of the discovery of circulating antibodies in pemphigus and in bullous pemphigoid. The etiologic concepts of these diseases as well as diagnosis and treatment have been affected.

With regard to etiology, the authors cite the available evidence indicating that the antibodies might be the cause of the disease in pemphigus and bullous pemphigoid. Although many factors speak in favor of this concept, the ultimate proof for it—namely, the passive transfer of the disease by means of its antibodies—may never be attained. Still, it can be said that lesions analogous to those of pemphigus vulgaris have been reproduced in animals by the experimental production of intercellular antibodies in such animals. Also, in addition to the evidence cited by the authors, it would seem that the favorable results obtained with methotrexate in the treatment of both pemphigus and bullous pemphigoid favor the concept of autoimmunity as a causative factor. In addition, the occasional coexistence of pemphigus with other immunological disorders, such as lupus erythematosus, rheumatoid arthritis and myasthenia gravis, indicates pemphigus too may be an autoimmune disorder, even though in most instances the additional immunologic disorder coexisting with pemphigus is silent and evident only by laboratory tests.

The diagnostic value of the demonstration of "antiepithelial" antibodies in pemphigus and of "basement zone" antibodies in bullous pemphigoid is considerable since these antibodies are specific for pemphigus and bullous pemphigoid, respectively. With adequate controls it is possible to avoid false positive results such as were obtained by the authors when fortuitously they used as substrate the esophagus of a rhesus monkey possessing blood-group-B substance. This resulted in fluorescence when serum from patients having anti-B isohemagglutinins in their blood was tested.

There is, however, a drawback in the antibody determination method for diagnostic purposes in that it may give negative results in the early stage of pemphigus or bullous pemphigoid when only a few lesions are present. Possibly, with improvement of the technique and the substitution of peroxidase-labeled antibodies for fluorescein-labeled antibodies, the incidence of false negative results can be reduced in the future. However, as was pointed out by the authors, it actually is not necessary to use indirect immunofluorescent testing for routine diagnostic purposes, since in most instances histologic examination is adequate for diagnostic clarification. Also, histologic examination enables one to dif-

ferentiate between pemphigus vulgaris and pemphigus foliaceus which, on indirect immunofluorescent examination, are indistinguishable.

Newcomer and Landau rightly emphasize that, even though there often is a correlation between the antibody titer and the severity of the disease, it is inadvisable to use determinations of the antibody titer as a guide for therapy. The clinical state of the patient is the only reliable guide.

They also point out that the greatest value of methotrexate in the treatment of pemphigus vulgaris lies not in the fact that occasionally in early cases it can completely replace prednisone, but rather that after the initial massive treatment with prednisone, the addition of methotrexate to the maintenance dose of the corticosteroid usually permits a gradual reduction in the maintenance dose and an earlier discontinuance of it. By reducing the incidence of serious and often fatal side effects of prednisone, methotrexate, particularly in patients with pemphigus vulgaris, has greatly improved the results of treatment over those obtained with prednisone alone and has further improved the prognosis of pemphigus vulgaris which at one time was almost always fatal.

WALTER F. LEVER, M.D.

*Professor and Chairman, Department of Dermatology
Tufts University School of Medicine
Boston*

"Right On!"

IN HIS "CONSIDERATIONS in Devising an Over-all Health Plan" submitted to the Department of Health, Education, and Welfare, and reprinted elsewhere in this issue, Dr. Russell Roth, the Speaker of the American Medical Association House of Delegates, is "right on." This concisely reasoned, thoughtful and accurate statement should not only be read, but carefully studied by practicing physicians, medical educators, health care planners, payors, providers, consumers and any others who may be in positions of influence with respect to the present health care "crisis" in the United States, or in California for that matter. Above all it should be read and pondered by legislators and other government officials who so often seem to create more problems than they solve by their no doubt well-intentioned legislative and administrative actions.

If Dr. Roth's "Considerations" should perchance be heeded by those in positions of power and influence in government and elsewhere, it could mark the beginning of what must be done if the health care problems of this nation are ever to be solved.

The AMA is to be congratulated upon having in its Speaker a spokesman of this caliber.

THE PAIN OF BRAIN TUMOR

Would you describe the characteristics of head pain due to a brain tumor or increased intracranial pressure?

"Head pain due to a tumor is practically never acute and never tremendously severe. It is dull and often continuous. When it is localized and to one side or the other, it's a very reliable sign that the lesion is to that side. Another characteristic of head pain related to increased intracranial pressure or a brain tumor is that more often than not, if it's on the posterior fossa, it will be localized toward the back and if it is more anterior, toward the front. It is often accentuated in early morning on arising. The patient who says he wakes up with a dull, rather continuous headache may well have a brain tumor or increased pressure. Frequently this headache, although dull, is rather continuous and is exaggerated by a straining at the stool or by changes in position."

—ELI S. GOLDENSOHN, M.D., New York City
Extracted from *Audio-Digest Internal Medicine*, Vol. 16, No. 16, in the Audio-Digest Foundation's subscription series of tape-recorded programs. For subscription information: 619 S. Westlake Ave., Los Angeles, Ca. 90057.